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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
KETTER, JAMES S

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 07/01/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/732,914	Applicant(s) CHEO ET AL.	
	Examiner James Ketter	Art Unit 1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-142 is/are pending in the application.

4a) Of the above claim(s) 55,61,74,75,101,102 and 124-142 is/are withdrawn from consideration.

5)☒ Claim(s) 22,47-54,77-100 and 103-107 is/are allowed.

6)☒ Claim(s) 1-8,11-19,21,23-34,38-46,56-60,62-68,70-73,76,108-112,115-123 is/are rejected.

7)☒ Claim(s) 69,113 and 114 is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6,10 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Applicant's election with traverse of Group I, claims 1-8, 11-19, 21-54, 56-60, 62-73, 76-100 and 103-123, in Paper No. 8, filed 16 April 2002, is acknowledged. The traversal is on the ground(s) that the search for the elected invention would encompass the search for the non-elected inventions. This is not found persuasive because the searches, while overlapping to some degree, would not be at all co-extensive. A reference anticipating one invention might be inapplicable to another, and vice versa.

The requirement is still deemed proper and is therefore made FINAL.

Claims 9, 10, 20, 55, 61, 74, 75, 101, 102 and 124-142 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 8.

Claims 35-37, 69, 113 and 114 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Claims 22, 47-54, 77-100 and 103-107 are allowed.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground

provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-6, 11-16, 21, 23-30, 32, 38, 39, 43-45, 56, 62-68, 70-73 and 76 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 6, 22 and 23 of U.S. Patent No. 6,277,608, as follows: instant claims 28-30 and 32 over patented claim 6; instant claims 5 and 26 over patented claim 22; instant claims 3 and 25 over patented claim 23; and the remaining instant claims over patented claim 1. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims encompass the respective patented claims, except in the case of instant claim 11, which is obvious over patented claim 1 in that it would have been obvious to have placed a nucleic acid clone in a vector into a host cell for manipulation, testing and storage or amplification, as such is and was the routine in the art for recombinant methods. The method of claim 11 and the patented method are related as combination and subcombination, and are not patentably distinct.

Claims 1, 2, 4, 6, 11-16, 21, 23, 24, 27, 38, 39, 43-45, 56, 62-68, 70-73 and 76 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 30 of U.S. Patent No. 5,888,732. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims encompass the patented claim, except in the case of instant claim 11, which is obvious over patented claim 30 in that it would have been obvious to have placed a nucleic acid clone in a

vector into a host cell for manipulation, testing and storage or amplification, as such is and was the routine in the art for recombinant methods. The method of claim 11 and the patented method are related as combination and subcombination, and are not patentably distinct.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1, 7, 8 and 17-19 are rejected under 35 U.S.C. 102(b) as being anticipated by Scott et al. (A, newly cited).

The instant claims are drawn to a method of recombining a population of nucleic acid molecules with a target nucleic acid, comprising mixing the population with the target, and using a recombinase to catalyze the reaction, followed by selection against the population and the target molecules.

Scott et al. teaches, e.g., at column 7, first full paragraph, recombination between a vector and the target chromosomal DNA, wherein recombination is directed by flanking loxP sites, and wherein negative selection is used to select against the vector sequences.

Claims 1, 7, 8 and 17-19 are rejected under 35 U.S.C. 102(e) as being anticipated by Piedrahita et al. (B, newly cited).

The instant claims are drawn to a method of recombining a population of nucleic acid molecules with a target nucleic acid, comprising mixing the population with the target, and using a recombinase to catalyze the reaction, followed by selection against the population and the target molecules.

Piedrahita et al. teaches, e.g., at the paragraph bridging columns 86 and 87, recombination between a vector and the target chromosomal DNA, wherein recombination is directed by a loxP site, and wherein a TK-neo cassette is used for negative selection against the vector sequences.

Claims 1-6, 11-16, 21, 23-34, 38, 39, 43-46, 56-60, 62-68, 70-73 and 76 are rejected under 35 U.S.C. 102(e) as being anticipated by Hartley et al. (C, newly cited).

The instant claims are drawn to a method of recombining a population of nucleic acid molecules with a target molecule or population, more narrowly claimed as occurring directed by two different recombination sites, more narrowly claimed that a regulatory sequence is present

on one of the nucleic acid molecules, more narrowly claimed that the recombination creates a nucleic acid which encodes a fusion protein,

Hartley et al. teaches, e.g., as summarized in Figure 1, joining two nucleic acid molecules using a recombinase, particularly using two different recombinases. At column 15, first paragraph, Hartley et al. teaches a variety of genes which may be encoded by one of the nucleic acid molecules, many of which inherently possess promoters and other regulatory sequences. Particularly taught are markers, including green fluorescent protein (GFP). At column 26, first full paragraph, Hartley et al. teaches the generation of a fusion protein using the recombination methods generally taught.

Claims 1-6, 11-16, 64-68, 70-73, 76, 108-112 and 120-123 are rejected under 35 U.S.C. 102(e) as being anticipated by Winter et al. (D, newly cited).

The instant claims are drawn to a method of recombining a population of nucleic acid molecules with a target molecule or population, more narrowly claimed that a regulatory sequence is present on one of the nucleic acid molecules, as well as to methods of expressing protein from a recombined nucleic acid molecule, using a suppressor tRNA in combination with a suppressible stop codon, more narrowly claimed that the protein is an antibody or single-chain antibody.

Winter et al. teaches, generally, the expression of recombinant, i.e., recombined antibodies. At column 14, lines 57-63, Winter et al. teaches that the vector expressing the heavy and light chains may be assembled using the Cre/LoxP system. At column 47, line 36, it is taught that the SupE suppressor tRNA system was used on the expression vector.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 23, 38 and 40-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hartley et al. (C) in view of Winter et al. (D).

The instant claims are drawn to a method of recombining a population of nucleic acid molecules with a target molecule or population, more narrowly claimed as occurring directed by two different recombination sites, wherein the nucleic acid molecules are libraries of light and heavy chains of antibodies.

Hartley et al. teaches, e.g., as summarized in Figure 1, joining two nucleic acid molecules using a recombinase, particularly using two different recombinases. However, Hartley et al. differs from the claimed invention in not teaching the expression of an antibody molecule or other binding protein with binding specificity.

Winter et al. generally teaches, e.g., as summarized in the Abstract, the co-expression of antibody proteins, e.g., light and heavy chains as heterodimers or fused as single-chain antibodies. At column 14, lines 57-63, it is taught that the co-expression vectors of the teachings of Winter et al. may be assembled using the Cre/LoxP system.

It would have been obvious to have employed the recombination methods taught by Hartley et al. to have assembled the co-expression vectors encoding antibody light and heavy chains, taught by Winter et al. One of ordinary skill in the art would have been motivated to express the antibodies of Winter et al. using the recombinase system of Hartley et al., as Winter et al. suggests using such a system.

Claims 23, 38 and 40-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hartley et al. (C) in view of Winter et al. (D), and further in view of either Hodges et al. (E, newly cited) or Baszczynski et al. (F, newly cited).

The instant claims are drawn to a method of recombining a population of nucleic acid molecules with a target molecule or population, more narrowly claimed as occurring directed by two different recombination sites, wherein the nucleic acid molecules are libraries of light and heavy chains of antibodies, wherein the recombinase .

Hartley et al. teaches, e.g., as summarized in Figure 1, joining two nucleic acid molecules using a recombinase, particularly using two different recombinases. However, Hartley et al. differs from the claimed invention in not teaching the expression of an antibody molecule or other binding protein with binding specificity, nor in specifically teaching recombinase systems other than attB/P or Cre/LoxP.

Winter et al. generally teaches, e.g., as summarized in the Abstract, the co-expression of antibody proteins, e.g., light and heavy chains as heterodimers or fused as single-chain antibodies. At column 14, lines 57-63, it is taught that the co-expression vectors of the teachings of Winter et al. may be assembled using the Cre/LoxP system.

(While it is noted that the instant claims were rejected, above, under 35 USC § 103, over Hartley et al. in view of Winter et al., only, certain embodiments encompassed by the instant claims are not thus rendered obvious by these references only.)

Hodges et al teaches, e.g., at column 5, third full paragraph, that any of a number of site-specific recombinase systems may be used to recombine nucleic acid molecules, showing the equivalency in the art of such recombinases. Particularly, FLP/FRT, Gin, Pin and R/RS are taught.

Baszczynski et al. teaches, e.g., at the paragraph bridging columns 3 and 4, that any of a number of site-specific recombinase systems may be used to recombine nucleic acid molecules, showing the equivalency in the art of such recombinases. Particularly, FLP/FRT, Cre, Int and R/RS are taught.

It would have been obvious to have employed the recombination methods taught by Hartley et al. to have assembled the co-expression vectors encoding antibody light and heavy chains, taught by Winter et al., using any known system of site-specific recombinase and associated recombination site One of ordinary skill in the art would have been motivated to express the antibodies of Winter et al. using the recombinase system of Hartley et al., as Winter et al. suggests using such a system. The motivation to have used any known recominase system

having come from the teachings of Hodges et al. or Baszczynski et al. of the equivalency of such site-specific recombinases.

Claims 1, 7, 8 and 17-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Scott et al. (A) or Piedrahita et al. (B), either taken in view of either Hodges et al. (E, newly cited) or Baszczynski et al. (F, newly cited).

Scott et al. was described above. While it is noted, as set forth above, that Scott et al. anticipates the instant claims, certain embodiments encompassed by the instant claims are not thus anticipated. With respect to these embodiments, Scott et al. does not teach the use of recombinase systems other than Cre/LoxP.

Piedrahita et al. was described above. While it is noted, as set forth above, that Piedrahita et al. anticipates the instant claims, certain embodiments encompassed by the instant claims are not thus anticipated. With respect to these embodiments, Scott et al. does not teach the use of recombinase systems other than Cre/LoxP.

Hodges et al teaches, e.g., at column 5, third full paragraph, that any of a number of site-specific recombinase systems may be used to recombine nucleic acid molecules, showing the equivalency in the art of such recombinases. Particularly, FLP/FRT, Gin, Pin and R/RS are taught.

Baszczynski et al. teaches, e.g., at the paragraph bridging columns 3 and 4, that any of a number of site-specific recombinase systems may be used to recombine nucleic acid molecules,

showing the equivalency in the art of such recombinases. Particularly, FLP/FRT, Cre, Int and R/RS are taught.

It would have been obvious to one of ordinary skill in the art to have selected any known system of site-specific recombinase and associated recombination site to have practiced the recombination method of Scott et al., the motivation having come from the teachings of Hodges et al. or Baszczynski et al. of the equivalency of such site-specific recombinases.

Claims 1-6, 11-16, 21, 23-34, 38, 39, 43-46, 56-60, 62-68, 70-73 and 76 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hartley et al. (C) in view of either Hodges et al. (E, newly cited) or Baszczynski et al. (F, newly cited).

Hartley et al. was described above. While it is noted, as set forth above, that Hartley et al. anticipates the instant claims, certain embodiments encompassed by the instant claims are not thus anticipated. With respect to these embodiments, Hartley et al. does not teach the use of recombinase systems other than Cre/LoxP.

Hodges et al teaches, e.g., at column 5, third full paragraph, that any of a number of site-specific recombinase systems may be used to recombine nucleic acid molecules, showing the equivalency in the art of such recombinases. Particularly, FLP/FRT, Gin, Pin and R/RS are taught.

Baszczynski et al. teaches, e.g., at the paragraph bridging columns 3 and 4, that any of a number of site-specific recombinase systems may be used to recombine nucleic acid molecules,

showing the equivalency in the art of such recombinases. Particularly, FLP/FRT, Cre, Int and R/RS are taught.

It would have been obvious to one of ordinary skill in the art to have selected any known system of site-specific recombinase and associated recombination site to have practiced the recombination method of Hartley et al., the motivation having come from the teachings of Hodges et al. or Baszczynski et al. of the equivalency of such site-specific recombinases.

Claims 1-6, 11-16, 64-68, 70-73, 76, 108-112 and 120-123 are rejected under 35 U.S.C. 103(a) as being unpatentable over Winter et al. (D) in view of either Hodges et al. (E, newly cited) or Baszczynski et al. (F, newly cited).

Winter et al. was described above. While it is noted, as set forth above, that Winter et al. anticipates the instant claims, certain embodiments encompassed by the instant claims are not thus anticipated. With respect to these embodiments, Hartley et al. does not teach the use of recombinase systems other than Cre/LoxP.

Hodges et al teaches, e.g., at column 5, third full paragraph, that any of a number of site-specific recombinase systems may be used to recombine nucleic acid molecules, showing the equivalency in the art of such recombinases. Particularly, FLP/FRT, Gin, Pin and R/RS are taught.

Baszczynski et al. teaches, e.g., at the paragraph bridging columns 3 and 4, that any of a number of site-specific recombinase systems may be used to recombine nucleic acid molecules, showing the equivalency in the art of such recombinases. Particularly, FLP/FRT, Cre, Int and R/RS are taught.

It would have been obvious to one of ordinary skill in the art to have selected any known system of site-specific recombinase and associated recombination site to have practiced the recombination method of Winter et al., the motivation having come from the teachings of Hodges et al. or Baszczynski et al. of the equivalency of such site-specific recombinases.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 115-119 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The preamble of claim 115 is drawn to determining a gene expression profile. However, the terminal step of the claimed process is drawn to determining a nucleic acid sequence. As such, it is not clear to what process the instant claim is actually drawn, and thus the metes and bounds of the instant claims are not clear.

With further respect to claim 115, "site" at line 5 should be "sites".

Certain papers related to this application may be submitted to the directly to the Examiner by facsimile transmission at (703) 746-5155. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993)(see 37 CFR ' 1.6(d)). To send the facsimile to the Art Unit instead, the Art

Unit 1636 Fax number is (703) 305-7939. NOTE: If Applicant does submit a paper by fax to this number, the Examiner must be notified promptly, to ensure matching of the faxed paper to the application file, and the original signed copy should be retained by Applicant or Applicant's representative. (703) 308-4242 or (703) 305-3014 may be used without notification of the Examiner, with such faxed papers being handled in the manner of mailed responses. Applicant is encouraged to use the latter two fax numbers unless immediate action by the Examiner is required, e.g., during discussions of claim language for allowable subject matter. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the Examiner with respect to the examination on the merits should be directed to James Ketter whose telephone number is (703) 308-1169. The Examiner normally can be reached on M-F (9:00-6:30), with alternate Fridays off.

Questions regarding formalities and processing of the case should be directed to Zeta Adams, whose telephone number is (703) 305-3291.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Remy Yucel, can be reached at (703) 305-1998.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1234.

Jsk
June 22, 2002

JAMES KETTER
PRIMARY EXAMINER